THE AMENDMENTS

Please enter the attached sequence listing (6 pages).

In the Specification:

Amend the paragraph starting on page 1, line 18:

Thus, the subject matter of the present invention relates to a protein which is suitable for inhibiting apoptosis, the protein comprising the amino acid sequence of figure 1 (SEQ ID NO:3) or an amino acid sequence differing therefrom by one or several amino acids.

Amend the paragraph starting on page 1, line 21:

The present invention is based on the applicant's finding that in animals, particularly mammals, more particularly human beings, a protein exists which can inhibit apoptosis. This protein comprises the amino acid sequence of figure 1 (SEQ ID NO:3) or an amino acid sequence differing therefrom by one or several amino acids. Furthermore, the applicant found that the protein interacts with the adapter protein FADD, so that the recruitment and the activation of the protease FLICE are inhibited at DISC.

Amend the paragraph starting on page 1, line 29:

(a) the DNA of figure 1 (SEQ ID NO:1) of a DNA differing therefrom by one or several base pairs,

Amend the paragraph starting on page 1, line 34:

The DNA of figure 1 (SEQ ID NO:1) was deposited with the DSM (Deutsche Sammlung von Mikroorganismen und Zellkulturen [German-type collection of microorganisms and cell cultures]) as C-FLIP/2/W23795 and C-FLIP/1/AA115792 under DSM 11488 and DSM 11487, respectively, on March 25, 1997.

Amend the paragraph starting on page 2, line 11:

A further subject matter of the present invention relates to an antibody directed against an

above protein and fusion protein, respectively. Such an antibody can be prepared by common methods. It may be polyclonal and monoclonal, respectively. For its preparation it is favorable to immunize animals – particularly rabbits or chickens for a polyclonal antibody and mice for a monoclonal antibody –with an above (fusion) protein or a fragment thereof. Further "boosters" of the animals can be effected with the same (fusion) protein or with fragments thereof. The polyclonal antibody can then be obtained from the animal serum and egg yolk, respectively. For the preparation of the monoclonal antibody, animal spleen cells are fused with myeloma cells. An antibody according to the invention, which is directed against a protein having the amino acid of figure 2 (SEQ ID NO:5), was deposited with the DSM as NF6 on April 1, 1998.

Amend the paragraph starting on page 2, line 39:
Fig. 1 shows the base sequence (SEQ ID NO:1) and the amino acid sequence (SEQ ID NO:3) derived therefrom and comprised by a FLIP protein according to the invention. The edged sequence shows a DED (death effector domain) region. The sequence of figure 1 is found in DSM 11488.

Amend the paragraph starting on page 2, line 43:
Fig. 2 shows the base sequence (SEQ ID NO:4) and the amino acid sequence (SEQ ID NO:5) derived therefrom and comprised by a FLIP protein according to the invention. The sequence of figure 2 is found in DSM 11487.

Amend the paragraph starting on page 3, line 3:
For the preparation of a FLIP protein according to the invention the DNA of fig. 1 (SEQ ID NO:1) is provided with BamHI linkers, subsequently excised using BamHI and inserted in the expression vector pQE8 (Diagen company) cleaved by BamHI. The expression plasmid pQ/FLIP is obtained. Such a plasmid codes for a fusion protein comprising 6 histidine residues (N terminus partner) and the FLIP protein of fig. 1 (SEQ ID NO:3) according to the invention (C terminus partner). PQ/FLIP is used for transforming E. coli SG 13009 (cf.

Gottesman, S. et al., J. Bacteriol. 148, (1981), 265-273). The bacteria are cultured in an LB broth with 10 μg/ml ampicillin and 25 μg/ml kanamycin and induced with 60 μM isopropyl-β-D-thiogalactopyranoside (IPTG) for 4 h. Lysis of the bacteria is achieved by the addition of 6 M guanidine hydrochloride. Thereafter, chromatography (Ni-NTA resin) is carried out with the lysate in the presence of 8 M urea in accordance with the instructions from the manufacturer (Diagen company) of the chromatography material. The bound fusion protein is eluted in a buffer having a pH of 3.5. After its neutralization, the fusion protein is subjected to 18% SDS polyacrylamide gel electrophoresis and stained with coomassie blue (cf. Thomas, J.O. and Kornberg, R.D., J. Mol. Biol. 149 (1975), 709-733).

Amend the paragraph starting on page 4, line 14:

(a) The DNA of figure 2 (SEQ ID NO:4) is provided with ExoR5-/XbaI linkers, subsequently excised using EcoRI and XbaI and inserted in the expression vector pEFrsFLAG cleaved by the same restriction enzymes. The expression plasmid pEFrsFLAG-FLIP is obtained. It codes for a fusion protein FLAG-FLIP from a FLAG-Tag (N terminus partner) and the FLIP protein of figure 2 (SEQ ID NO:5) according to the invention (C terminus partner). PEFrsFLAG-FLIP is used for the transfection of the human cells BJAB. Extracts are obtained from transfected cells and separated electrophoretically on an SDS polyacrylamide gel. Then, a Western blot method is carried out in which a monoclonal antibody of Example 2 is used for detecting the expressed FLIP protein. An anti-mouse antibody is used for the detection of antibody binding (cf. figure 3A).